REMARKS

The last remaining issue in this case is whether claims 1-4, 8, 9, and 23-25 are anticipated by Hasan *et al.* (Journal of General Virology 1997; 78: 2873-2820). For the following reasons, applicants respectfully traverse this rejection:

The Office states:

> Hasan et al. anticipate a recombinant Sendai virus vector that expresses the firefly luciferase gene between the N protein and the 5' end of the RNA genome. The recombinant Sendai virus genome is expressed in a DNA expression vector, see Figure 1 on page 2815.
>
> * * * *
>
> Applicant states that Hasan et al. appears to show that the luciferase gene is inserted 5' to the N gene. Applicant describes the transcription of the described RNA of Hasan et al. and concludes that the luciferase gene of Hasan et al. is actually located 3' to the N gene.
>
> Applicant's arguments have been considered, but are found unpersuasive. The examiner is unable to understand applicant's position because the statement that antigenomic RNA is generated from the plasmid vector is incorrect because **it is actually an anti-sense RNA strand that is generated**. The reference clearly shows that the luciferase gene is upstream, i.e. 5', to the viral genes, which are present in the order recited in claim 3, see Figure 1 on page 2815 (emphasis added)

Because the Office fails to recognize the difference between viruses of the present invention and the virus of Hasan *et al.*, applicants traverse this rejection.

The Office's statement that "it is actually an anti-sense RNA strand that is generated [from the plasmid]" is incorrect. Referring to Appendix 1, the RNA shown at the bottom of the Fig. 1 of Hasan *et al.* is "SeV/luc antigenomic RNA (17112 nt)"

(underline added). The legend of Fig. 1 of Hasan *et al.* clearly indicates that "the resulting plasmid gives rise to an antigenomic SeV RNA" (underline added). The antigenomic RNA is therefore a sense RNA, not an anti-sense RNA. The Office has consequently erred in its analysis and in rejecting the claims.

Applicants first direct the examiner's attention to Appendix 2 (Lamb, R.A. and Kolalofsky, D., Paramyxoviridae: the viruses and their replication, *in* Fields Virology, 3rd ed., B.N. Feidls et al. (eds.), Lippincott-Raven Publishers, Philadelphia, 1996, page 1190-1192), which shows the life cycle of paramyxovirus (see Fig. 10 on page 1191). Paramyxovirus has an anti-sense RNA as the genomic RNA. Once the paramyxovirus infects a cell, the anti-sense RNA (shown as "GENOME (-)" in FIG. 10) is transcribed into the sense RNA (shown as "ANTIGENOME (+)" in FIG. 10). Consequently, both the anti-sense and sense RNAs are amplified in the cell, and only the anti-sense RNA is incorporated into the virus.

The recombinant virus of the present invention is generated essentially by the same steps as described in Appendix 2. In Appendix 3, sense RNA (i.e., the antigenomic RNA) is transcribed from the plasmid vector. Viral proteins required for the amplification of anti-sense and sense RNAs are also provided from the plasmid vectors (i.e., N, L, and P proteins). After the formation of an RNP complex that includes sense-RNA and viral proteins has occurred, the anti-sense and sense RNAs are then amplified in the cell. Following the same steps as the natural virus life cycle shown in Appendix 2,

recombinant viruses having an anti-sense RNA (genomic RNA) are generated.

A comparison between the viruses of the present invention and Hasan *et al.* is depicted in Appendix 4. This comparison clearly demonstrates that the viruses of the present invention are distinct from the virus of Hasan *et al.* First, Hasan's antigenomic RNA contains a luciferase gene at the 5' end of the NP gene. In contrast, the claimed vector does not give rise to a foreign gene that is positioned 5' to the NP gene in antigenomic RNA. Second, following the paramyxovirus life cycle, Hasan's antigenomic RNA is produced from a genomic (anti-sense) RNA. In Hasan's anti-sense RNA, the luciferase gene is positioned 3' to the NP gene, i.e., between the NP gene and the 3' end of the genomic (anti-sense) RNA. Hasan therefore does not describe "a foreign gene that is positioned 5' to a gene encoding a viral protein in the negative strand genomic RNA ..." as required by the claims. Given such differences, Hasan cannot anticipate the claimed invention, and the § 102 rejection should be withdrawn.

Sequence Requirements

Claim 24 was objected to for failing to adhere to the requirements of the sequence rules. To address the Examiner's concern, applicants have amended this claim to indicate that the additional E-I-S sequence includes the corresponding RNA sequence of SEQ ID NO:33.

CONCLUSION

Applicants submit that this case is now in condition for allowance, and such action is respectfully requested.

Enclosed is a petition to extent the period for replying for three months, to and including November 20, 2003. Also enclosed is a Notice of Appeal, in which applicants respectfully appeal the final rejection of the pending claims.

If there are any additional charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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